

**Table 4.** Differential expression of Apo E isoforms in AD patients versus contrast groups.

| Apo E NPI | PI   | MW (kDa) | 6 AD vs. 6 D   | 6 AD vs. 6 FTD | 6 AD vs. 10 FTD | 6 AD vs. 4 VAD | 6 AD vs. 4 VAD | Aa # start-end    | Peptide sequence # | Seq ID No. |
|-----------|------|----------|----------------|----------------|-----------------|----------------|----------------|-------------------|--------------------|------------|
| 34        | 5.11 | 35.2     | ↓              | =              | =               | =              | =              | 270-278           | LQAEAFQAR          | 1          |
|           |      |          |                |                |                 |                |                | 259-269           | AKLEEQQQIR         | 2          |
|           |      |          |                |                |                 |                |                | 166-175           | LLRDADDLQK         | 3          |
|           |      |          |                |                |                 |                |                | 19-33             | KVEQAVETEPEPELR    | 4          |
| 35        | 5.32 | 34.3     | ↓              | nd             | nd              | nd             | nd             | 270-278           | LQAEAFQAR          | 1          |
|           |      |          |                |                |                 |                |                | 259-269           | AKLEEQQQIR         | 2          |
|           |      |          |                |                |                 |                |                | 199-207           | GPLVQEGR           | 5          |
|           |      |          |                |                |                 |                |                | 301-317 (C-term.) | VQAAVGTSAAAPVPSDNH | 6          |
| 72        | 5.07 | 15.8     | =              | =              | nd              | nd             | nd             | 199-207           | GPLVQEGR           | 5          |
|           |      |          |                |                |                 |                |                | 270-278           | LQAEAFQAR          | 1          |
|           |      |          |                |                |                 |                |                | 259-269           | AKLEEQQQIR         | 2          |
| 73        | 5.11 | 15.8     | =              | =              | =               | =              | =              | 270-278           | LQAEAFQAR          | 1          |
| 74        | 4.91 | 15.8     | =              | =              | =               | =              | ↓              | 199-207           | GPLVQEGR           | 5          |
|           |      |          |                |                |                 |                |                | 270-278           | LQAEAFQAR          | 1          |
|           |      |          |                |                |                 |                |                | 259-269           | AKLEEQQQIR         | 2          |
|           |      |          |                |                |                 |                |                | 210-224           | AATVGSLAGQPLQER    | 7          |
|           |      |          |                |                |                 |                |                | 138-152           | GEVQAMLGQSTEELR    | 8          |
|           |      |          |                |                |                 |                |                | 94-108            | SELEEQLTTPVAEETR   | 9          |
|           |      |          |                |                |                 |                |                | 301-317 (C-term.) | VQAAVGTSAAAPVPSDNH | 6          |
| 75        | 5.09 | 15.1     | =              | nd             | nd              | nd             | nd             | 138-152           | GEVQAMLGQSTEELR    | 8          |
|           |      |          |                |                |                 |                |                | 19-33             | KVEQAVETEPEPELR    | 4          |
|           |      |          |                |                |                 |                |                | 270-278           | LQAEAFQAR          | 1          |
| 41        | 5.07 | 15.3     | ↓              | nd             | nd              | nd             | nd             | 19-33             | KVEQAVETEPEPELR    | 4          |
|           |      |          |                |                |                 |                |                | 270-278           | LQAEAFQAR          | 1          |
| 76        | 5.24 | 13.8     | = $\downarrow$ | ↓              | =               | =              | ↓              | 210-224           | AATVGSLAGQPLQER    | 7          |
| 77        | 4.96 | 12.4     | = $\uparrow$   | =              | =               | =              | =              | 259-269           | AKLEEQQQIR         | 2          |
| 52        | 5.30 | 33.8     | ↓              | nd             | nd              | nd             | nd             | 270-278           | LQAEAFQAR          | 1          |

**Table 4.** Differential expression of Apo E isoforms in AD patients versus contrast groups.

| Apo E<br>NPI | pI   | MW<br>(kDa) | 6 AD vs.<br>6 D | 6 AD<br>vs.<br>10 FTD | 6 AD vs.<br>6 FTD | 6 AD vs.<br>4 VAD | Aa #<br>start-end | Peptide sequence #  | Seq ID<br>No.                                 |
|--------------|------|-------------|-----------------|-----------------------|-------------------|-------------------|-------------------|---|---|
| 60           | 5.38 | 15.6        |                 |                       |                   |                   |                   | 199-207<br>259-269  | 5<br>2  |
| 66           | 5.17 | 30.         | ↓<br>QL         | nd                    | nd                | nd                | nd                | AKLEEQQQIR<br>ALMDETMKELK<br>KVEQAVETEPEPEL<br>LGPLVEQGR<br>AYKSELLEEQLTPVAAEETR<br>LSKELQAAQAR<br>AATVGSLAGQPLQER<br>AKLEEQQQIR<br>LQAEAFQAR | 10<br>4<br>5<br>11<br>12<br>7<br>2<br>1<br>12 |
| 11           | 5.22 | 35.3        | nd              | ↓QL                   | nd                | nd                | nd                | 199-207<br>259-269<br>270-278<br>19-33<br>91-109<br>111-121<br>210-224<br>259-269<br>270-278  | 5<br>2<br>1<br>4<br>11<br>12<br>7<br>2<br>1   |

Only quantitative results are showed (with the exception of NPI 66 and NPI 11, where only a qualitative difference (QL) was found).

↓: down-regulated in AD {↓: p<0.05; =↓: p < 0.07}

↑: upregulated in AD {↑: p<0.05; =↑: p<0.07}

=: no significant difference

#: peptide sequences covered by MS analysis

nd: not detected

**Table 5.** Identification of the protein spots that were altered between the studied groups.

| Spot exp1 | Spot exp2 | Peptide   | Seq ID No.   | aa  | Identification in database  | ID number database |
|-----------|-----------|---|--|---|---|--------------------|
| 2713      | 674       | TDTSHHDQDHPTTFNK<br>LVDKFLEDVK<br>FLEDVKK<br>KQINDYVEK<br>QINDYVEK<br>DTEEEDFHVDQATTVK (M1A allele)<br>DTEEEDFHVDQVTTVK (M1V allele)<br>LQHLENELTHDITK<br>FLENEDR<br>FLENEDRR<br>SASLHLPK<br>LSITGTYDLK<br>SVLGQLGITK<br>VFSNGADLSGVTEEAPLK<br>AVLTIDEK<br>TDTSHHDQDHPTTFNK<br>FLEDVKK<br>KQINDYVEK<br>QINDYVEK<br>DTEEEDFHVDQATTVK (M1A allele)<br>DTEEEDFHVDQVTTVK (M1V allele)<br>LSSWVLLMK + 1 Oxidation (M)<br>FLENEDR<br>FLENEDRR<br>SASLHLPK<br>LSITGTYDLK<br>SVLGQLGITK<br>VFSNGADLSGVTEEAPLK | 13<br>14<br>15<br>16<br>17<br>18<br>19<br>20<br>21<br>22<br>23<br>24<br>25<br>26<br>27<br>13<br>15<br>16<br>17<br>18<br>19<br>28<br>21<br>22<br>23<br>24<br>25<br>26<br>27<br>13<br>15<br>16<br>17<br>18<br>19<br>28<br>21<br>22<br>23<br>24<br>25<br>26 | 35-49<br>150-159<br>154-160<br>179-187<br>180-187<br>226-241<br>226-241<br>284-298<br>299-305<br>299-306<br>307-314<br>315-324<br>325-334<br>335-352<br>360-367<br>35-49<br>154-160<br>179-187<br>180-187<br>226-241<br>226-241<br>259-267<br>299-305<br>299-306<br>307-314<br>315-324<br>325-334<br>335-352<br>35-49<br>154-160<br>179-187<br>180-187<br>226-241<br>226-241<br>259-267<br>299-305<br>299-306<br>307-314<br>315-324<br>325-334<br>335-352 | Alpha-1-antitrypsin<br>Alpha-1-antitrypsin<br>Alpha-1-antitrypsin | P01009<br>P01009   |
| 4704      | 353       |   |  |   |   |                    |

**Table 5.** Identification of the protein spots that were altered between the studied groups.

| Spot exp1 | Spot exp2 | Peptide  | Seq ID No. aa  | Identification in database   | ID number database   |
|-----------|-----------|--|--|--|--|
| 4705      | 355       | AVLTIDEK<br>LGMFNIQHQCK (Cys-CAM)<br>QNDYVEK<br>LSITGTYDLK<br>SVLQLQLGITK<br>VFSNNGADLSSGVTEEAPLK<br>LLELTGPK<br>ATWSGAVLAGR<br>FALVREDR<br>CLAPLEGAR (cys-CAM + ox)<br>FALVREDR<br>LETPDFQLFK<br>ATWSGAVLAGR<br>LLELTGPK<br>EVPLNTIHFMRG + 1 Oxidation (M)<br>DVVSQFEGSALGK<br>VQPYLDDFQK<br>[916.56] <sup>†</sup> ALKED[360.25] <sup>†</sup> (aa 208 : N → D)<br>ATEHLSTLSEK<br>AKPALEDLR<br>LSPLGEEMR + 1 Oxidation (M) | 27<br>29<br>17<br>24<br>25<br>26<br>30<br>31<br>32<br>33<br>32<br>34<br>31<br>30<br>36<br>35<br>36<br>37<br>38<br>39<br>40<br>41<br>42<br>43<br>44<br>45<br>46<br>47<br>36 | 360-367<br>248-257<br>180-187<br>315-324<br>325-334<br>335-352<br>86-93<br>386-396<br>313-320<br>304-312<br>313-320<br>32-41<br>386-396<br>86-93<br>446-457<br>52-64<br>121-130<br>201-212<br>220-230<br>231-239<br>165-173<br>185-195<br>70-83<br>48-64<br>202-212<br>240-250<br>143-155<br>52-64<br>Apolipoprotein A-I | P01009<br>P01009<br>Alpha-1-antitrypsin<br>Alpha-1-antitrypsin<br>P04217<br>P04217<br>Alpha-1B-glycoprotein<br>Alpha-1B-glycoprotein<br>P04217<br>P04217<br>Alpha-1B-glycoprotein<br>Alpha-1B-glycoprotein<br>P04217<br>P04217<br>Antithrombin-III<br>Apolipoprotein A-I<br>P01008<br>P02647<br>P02647 |
| 7206      |           |  |  |  |  |
| 4801RBH   | 375       |  |  |  |  |
| 4803      |           |  |  |  |  |
| 1RBH      |           |  |  |  |  |
| 901RBH    |           |  |  |  |  |
| 5702      | 149       |  |  |  |  |
| 6102      |           |  |  |  |  |
| 6303      | 146       |  |  |  |  |

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| Spot exp1 | Spot exp2 | Peptide  | Seq ID No. aa | Identification in database | ID number database |
|-----------|-----------|--|---------------|----------------------------|--------------------|
|           |           | VQPYLDDFQK   | 37            | 121-130                    |                    |
|           |           | [916.56] <sup>+</sup> ALKED[360.27] <sup>+</sup> (aa208 : N → D) | 38            | 201-212                    |                    |
|           |           | ATEHLSTLSEK  | 39            | 220-230                    |                    |
|           |           | LSPLGEEMRDR + 1 Oxidation (M)                                    | 48            | 165-175                    |                    |
|           |           | LSPLGEEMR + 1 Oxidation (M)                                      | 41            | 165-173                    |                    |
|           |           | THLAPYSDEL R   | 42            | 185-195                    |                    |
|           |           | DSGRDYYVSQFEGSALGK   | 44            | 48-64                      | Apolipoprotein A-I |
|           |           | DYVSQFEGSALGK  | 36            | 52-64                      | P02647             |
|           |           | [1315.83] <sup>+</sup> DNDDDSVTSTFSK (aa 74: W → D)              | 49            | 70-83                      |                    |
|           |           | QEMSKDLEEVK + 1 Oxidation (M)                                    | 50            | 108-118                    |                    |
|           |           | VQPYLDDFQK   | 37            | 121-130                    |                    |
|           |           | VQPYLDDFQKK  | 51            | 121-131                    |                    |
|           |           | LSPLGEEMR + 1 Oxidation (M)                                      | 41            | 165-173                    |                    |
|           |           | LSPLGEEMRDR + 1 Oxidation (M)                                    | 48            | 165-175                    |                    |
|           |           | THLAPYSDEL R   | 42            | 185-195                    |                    |
|           |           | LEALKED[360.25] <sup>+</sup> (aa 208 : N → D)                    | 52            | 202-212                    |                    |
|           |           | LEALKENG GAR   | 45            | 202-212                    |                    |
|           |           | ATEHLSTLSEK  | 39            | 220-230                    |                    |
|           |           | AKPALEDLR  | 40            | 231-239                    |                    |
|           |           | DLATVYVVDV LK  | 53            | 237-247                    |                    |
|           |           | QGLLPVLESFK  | 46            | 240-250                    |                    |
|           |           | QKLHELQE K (E → pyroglutamic acid)                               | 54            | 156-164                    |                    |
|           |           | VEPLRAELQE GAR   | 47            | 143-155                    |                    |
|           |           | LLDNWDSVTSTFSK   | 43            | 70-83                      |                    |
|           |           | DEPPQSPPWDR + 1 Oxidation (W)                                    | 55            | 25-34                      |                    |
|           |           | DLATVYVVDV LK  | 53            | 37-47                      |                    |
|           |           | VSFLSALEEYTK   | 56            | 251-262                    |                    |
| 7101      | 285       | KWQEEMEL YR + 1 Oxidation (M)                                    | 57            | 131-140                    |                    |

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| Spot exp1 | Spot exp2 | Peptide                      | Seq ID No. aa | Identification in database | ID number database  |
|-----------|-----------|------------------------------|---------------|----------------------------|---------------------|
| 4310      | 144       | THLAPYSDELR                  | 42            | 185-195                    | Apolipoprotein A-I  |
|           | 143       | THLAPYSDELR                  | 42            | 185-195                    | Apolipoprotein A-I  |
| 4606+4605 |           | LGEVNTYAGDLQK                | 58            | 66-78                      | Apolipoprotein A-IV |
|           |           | LLPHANEVSQK                  | 59            | 113-123                    |                     |
|           |           | QLTPYAQR                     | 60            | 156-163                    |                     |
|           |           | IDQNVEELKGR                  | 61            | 190-200                    |                     |
|           |           | LTPYADEFK                    | 62            | 201-209                    |                     |
|           |           | ISASAEELR                    | 63            | 256-264                    |                     |
|           |           | LAPLAEEDVR                   | 64            | 267-275                    |                     |
|           |           | ALVQQMEQLR + 1 Oxidation (M) | 65            | 317-326                    |                     |
|           |           | LEPYADQLR                    | 66            | 135-143                    | Apolipoprotein A-IV |
|           |           | IDQNVEELKGR                  | 61            | 190-200                    |                     |
|           |           | LTPYADEFK                    | 62            | 201-209                    |                     |
|           |           | IDQTVEELR                    | 67            | 212-220                    |                     |
|           |           | ISASAEELR                    | 63            | 257-264                    |                     |
|           |           | LAPLAEEDVR                   | 64            | 267-275                    |                     |
|           |           | ALVQQMEQLR + 1 Oxidation (M) | 65            | 317-326                    |                     |
|           |           | RVEPYGENFNK                  | 68            | 306-317                    |                     |
|           |           | SLAPYAQDTQEK                 | 69            | 222-233                    |                     |
|           |           | LGEVNTYAGDLQK                | 58            | 66-78                      |                     |
|           |           | KVEQAVETEPEPELRL             | 4             | 19-33                      | Apolipoprotein E    |
|           |           | AYKSELEEQQLTPVAEETR          | 11            | 91-109                     |                     |
|           |           | LSKELQAAQAR                  | 12            | 111-121                    |                     |
|           |           | AATVGSLAGQPLQER              | 7             | 210-224                    |                     |
|           |           | AKLEEQAQQIR                  | 2             | 259-269                    |                     |
|           |           | LQAEAFQAR                    | 1             | 270-278                    |                     |
|           |           | LQAEAFQAR                    | 1             | 270-278                    | Apolipoprotein E    |
|           |           | AKLEEQAQQIR                  | 2             | 259-269                    |                     |

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| Spot<br>exp1 | Spot<br>exp2 | Peptide                         | Seq ID No. | aa      | Identification in database | ID number<br>database |
|--------------|--------------|---------------------------------|------------|---------|----------------------------|-----------------------|
|              |              | LLRIDADDLQK<br>KVEQAVETEPEPELR  | 3          | 166-175 |                            |                       |
| 114          |              | LQAEAFQAR<br>AKLEEQQQIR         | 4          | 19-33   |                            |                       |
|              |              | LGPLVEQGR<br>VQAAVGTSAAAPVPSDNH | 1          | 270-278 | Apolipoprotein E           | P02649                |
|              |              | LGPLVEQGR                       | 2          | 259-269 |                            |                       |
|              |              | LGPLVEQGR                       | 5          | 199-207 |                            |                       |
| 272          |              | KVEQAVETEPEPELR                 | 6          | 301-317 |                            |                       |
| 862          |              | LQAEAFQAR                       | 5          | 199-207 | Apolipoprotein E           | P02649                |
| 681          |              | LGPLVEQGR                       | 5          | 199-207 | Apolipoprotein E           | P02649                |
| 480          |              | KVEQAVETEPEPELR                 | 4          | 19-33   | Apolipoprotein E           | P02649                |
|              |              | LQAEAFQAR                       | 1          | 270-278 | Apolipoprotein E           | P02649                |
|              |              | LGPLVEQGR                       | 5          | 199-207 | Apolipoprotein E           | P02649                |
|              |              | AKLEEQQQIR                      | 2          | 259-269 |                            |                       |
| 3405         |              | ALMDETMKELK + 2 Oxidations (M)  | 70         | 80-90   |                            |                       |
| 3505         |              | ELDESQVAER                      | 71         | 326-336 | Apolipoprotein J           | P10909                |
| 4401         | 323          | ELDESQVAER                      | 71         | 326-336 | Apolipoprotein J           | P10909                |
|              |              | ELDESQVAER                      | 71         | 326-336 | Apolipoprotein J           | P10909                |
|              |              | KYNELLK                         | 72         | 340-346 |                            |                       |
|              |              | FMETVAAEK + 1 Oxidation (M)     | 73         | 430-437 |                            |                       |
| 5302         | 108          | ELDESQVAER                      | 71         | 326-336 | Apolipoprotein J           | P10909                |
|              |              | EILSVDCTNNPSQAK + 1 (cys-CAM)   | 74         | 307-322 | Apolipoprotein J           | P10909                |
| 8601         |              | TLLSNLEAK                       | 75         | 69-78   |                            |                       |
|              |              | IDSLLENDR                       | 76         | 159-167 |                            |                       |
| 5202         |              | ASSIDELFQDR                     | 77         | 183-194 |                            |                       |
|              |              | AGALNSNDAFVLK                   | 78         | 585-597 | Gelsolin                   | P06396                |
| 6404         |              | YIETDPANR                       | 79         | 730-738 |                            |                       |
|              |              | AGALNSNDAFVLK                   | 78         | 585-597 | Gelsolin                   | P06396                |
| 5004         | 411          | TGAQELLR                        | 80         | 616-623 |                            |                       |
|              |              | TEGDGVYTNDKK                    | 81         | 60-72   | Haptoglobin-1/2            | P00737                |

**Table 5.** Identification of the protein spots that were altered between the studied groups.

| Spot<br>exp1 | Spot<br>exp2 | Peptide   | Seq ID No.<br>aa               | Identification in database           | ID number<br>database                |
|--------------|--------------|---|--------------------------------|--------------------------------------|--------------------------------------|
|              |              | TEGDGVYTLLNDKKQWINK + 1 ox (W)  | 82<br>60-77<br>119-136         |                                      | P00738<br>P00737<br>P00738<br>P02790 |
| 5903RBH      |              | NFPSPVDAAFR<br>GGYTLVSGYPK  | 83<br>84<br>92-102<br>333-343  | Hemopexin                            | P00738<br>P02790                     |
| 8902RBH      |              | NFPSPVDAAFR<br>QGHNSVFLIK   | 83<br>85<br>92-102<br>103-112  | Hemopexin                            | P02790                               |
|              |              | DYFMPCPGK + 1 (cys-CAM + ox) + 1<br>ox (M)                                  | 86<br>226-234                  |                                      |                                      |
| 4701RBH      |              | GGYTLVSGYPK<br>SAVQGPPEK  | 84<br>87<br>333-343<br>169-177 | Ig alpha-1 chain C region<br>(heavy) | P01876                               |
|              |              | QEPSQGTTFAVTSILR<br>TPLTATLSK   | 88<br>89<br>283-299<br>213-221 | Ig alpha-1 chain C region<br>(heavy) | P01876                               |
| 4804         |              |   | 90<br>65-75<br>188-196         | Kininogen                            | P01042                               |
| 4702         |              | TVGSDTFYSFK<br>QVVAGLNFR<br>YFDFVAR   | 91<br>92<br>317-324            |                                      |                                      |
|              |              | APEAQVSVQPNFQQDK  | 93<br>23-38                    | Prostaglandin-H2 D-<br>isomerase     | P41222                               |
| 8101         |              | TMLQPAGSLGSYSYR + 1 Oxidation (M)   | 94<br>95<br>169-185            |                                      |                                      |
|              |              | AQGFTEDTIVFLPQTDK<br>[1617.85] <sup>+</sup> EAQVSVQPNF[518-26] <sup>+</sup> | 96<br>23-38                    | Prostaglandin-H2 D-<br>isomerase     | P41222                               |
| 9209         |              |   |                                |                                      |                                      |
| 6001         |              | TMLQPAGSLGSYSYR + 1 Oxidation (M)   | 94<br>93-108                   |                                      | P02766                               |
| 7102         |              | AADDITDEPFASGK (aa 61 : W → D)  | 97<br>56-68                    | Transthyretin                        | P02766                               |
| 7108         | 274          | [603.41]PLMVK   | 98<br>21-35                    | Transthyretin                        | P02766                               |
|              |              | GPTGTGESKCPPLMVK (Cys(O <sub>3</sub> H))                                    | 99<br>21-35                    | Transthyretin                        | P02766                               |

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| Spot exp1 | Spot exp2 | Peptide  | Seq ID No. | aa      | Identification in database | ID number database |
|-----------|-----------|--|------------|---------|----------------------------|--------------------|
|           |           | GPTGTGESKCPPLMVK (Cys(O <sub>3</sub> H)/M : oxidation to sulphone) | 99         | 21-35   |                            |                    |
|           |           | AADDTWEPFASGK (W + 2*16 Da)  | 100        | 56-68   |                            |                    |
|           |           | AADDTDEPFASGK (aa 61 : W → D)                                      | 97         | 56-68   |                            |                    |
|           |           | AADDTWEPFASGK  | 100        | 56-68   |                            |                    |
|           |           | KAADDTWEPFASGK   | 102        | 55-68   |                            |                    |
|           |           | TSESGELHGLTTTEEFVEGIYK   | 103        | 69-90   |                            |                    |
|           |           | HLSLLTTLNSR  | 104        | 208-218 | Vitamin D-binding protein  | P02774             |
|           |           | YTFELSR  | 105        | 346-352 |                            |                    |
|           |           | THLPEVFLSK   | 106        | 354-363 |                            |                    |
|           |           | VLEPTLK  | 107        | 364-370 |                            |                    |
|           |           | ELSSFIDK   | 108        | 395-402 |                            |                    |
|           |           | VCQQYAAAYGEK (cys-CAM + ox)  | 109        | 219-229 | Vitamin D-binding protein  | P02774             |
|           |           | VMDKYTFELSR + 1 Oxidation (M)                                      | 110        | 342-352 |                            |                    |
|           |           | YTFELSR  | 105        | 346-352 |                            |                    |
|           |           | THLPEVFLSK   | 106        | 354-363 |                            |                    |
|           |           | VLEPTLK  | 107        | 364-370 |                            |                    |
|           |           | [1433 61] <sup>†</sup> CCDVVEDSTTCFNAK (1 cys-CAM + ox, 2 Dha)     | 111        | 371-388 |                            |                    |
|           |           | ELSSFIDK   | 108        | 395-402 |                            |                    |
|           |           | AKLPDATPK  | 112        | 428-436 |                            |                    |
|           |           | AGEVQEPELR   | 113        | 239-248 | Zinc-alpha-2-glycoprotein  | P23311             |
|           |           | QDPPSVVVTSHQAPGEK  | 101        | 201-217 |                            |                    |
| 360IRBH   |           |  |            |         |                            |                    |
| 4411      |           |  |            |         |                            |                    |
| 2402      | 88        |  |            |         |                            |                    |